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131. (Amended) The method according to claim 138,  
wherein said gene or fragment thereof is a viral replicase gene or a  
fragment thereof.

132. (Amended) The method according to claim 138,  
wherein said gene or fragment thereof contains a binding site for a  
replicase enzyme.

### REMARKS

The status of the claims, following entry of the present amendment, is as follows: claims 1-21 are pending; claims 30, 60, 65, 67, 68, 71, 74-76, 79, 90-104, 113, 115, 116, 119, 122-124, 127-130, and 133 are cancelled; and claims 22-29, 31-59, 61-64, 66, 69, 70, 72, 73, 77, 78, 80-89, 105-112, 114, 117, 118, 120, 121, 125, 126, 131, 132, and 134-153 are pending.

Descriptive support for new reissue claims 134-153 is indicated in the table below.

#### Reissue Claims

134. A method of producing virus resistant plants comprising:

introducing into a plant cell a DNA coding for a gene, or fragment thereof, of the virus which when introduced into plant cells inhibits pathogenesis by the virus, wherein said DNA is in a sense direction and codes for a protein or polypeptide of said virus other than a coat protein;

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Page 15, lines 54-57 discloses that plants can be readily protected from viruses using the method of the invention.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

"Gene" is defined to encompass both DNA sequences that code for peptide gene product and other DNA sequences that form a functional part of a chromosome or plasmid. Page 12, lines 23-26.

"Gene fragment" encompasses entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are

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incomplete parts of a single gene. Page 12, lines 19-23.

"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

Page 11, lines 63-66 states that, in general, genetic information (DNA or RNA) from any virus is isolated using standard procedures and cleaved into pieces of varying lengths. Page 12, lines 2-3 discloses that DNA fragments are typically obtained using restriction endonuclease enzymes.

Page 5, line 66 to Page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme.

See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

recovering transformed plant cells; and

Recovering transformed cells with increased resistance to Q $\beta$  infection is disclosed in the example discussed at Page 18, line 60 to page 19, line 39. See also page 8, lines 12-19 (methods described for engineering resistance

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regenerating virus resistant plants from said transformed cells.

135. A recombinant DNA molecule comprising:

a promoter which is functional in plant cells and

a DNA sequence which encodes a protein or polypeptide native to a virus, other than a coat protein or polypeptide, operably linked to the promoter in a sense direction, wherein said recombinant DNA molecule when introduced into the plant cells will prevent the propagation of the virus.

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to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 15, lines 11-12 indicates that whole transformed plants can be regenerated in numerous plant species.

The example discloses a plasmid, which is a recombinant double stranded DNA molecule, for use in production of the coat protein. Page 18, lines 40-47.

Page 12, lines 14-17 refers to use of appropriate 5' sequences to ensure transcription (*i.e.*, RNA production).

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make *E. coli* resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role.

The example discusses expression of the coat protein under lac operator control. Page 18, lines 42-45. Implicit in this discussion is the production of an RNA sequence encoding the protein.

See also Page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 7, lines 27-37 discloses the use of a cloned Q $\beta$  replicase binding site. See also page 8, lines 12-19 (methods described for

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136. A virus resistant plant comprising:

a recombinant DNA molecule having a gene, or fragment thereof, isolated from the virus, wherein said gene, or fragment thereof, is in a sense direction and encodes a protein or polypeptide of the virus other than a coat protein or polypeptide, wherein said recombinant DNA molecule when introduced into plant cells inhibits pathogenesis by the virus.

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engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

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"Gene" is defined to encompass both DNA sequences that code for peptide gene product and other DNA sequences that form a functional part of a chromosome or plasmid. Page 12, lines 23-26.

"Gene fragment" encompasses entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are incomplete parts of a single gene. Page 12, lines 19-23.

"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

Page 11, lines 63-66 states that, in general, genetic information (DNA or RNA) from any virus is isolated using standard procedures and cleaved into pieces of varying lengths. Page 12, lines 2-3 discloses that DNA fragments are typically obtained using restriction endonuclease enzymes.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used

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to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural, role. The example discusses expression of the coat protein under lac operator control. Page 18, lines 42-45. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); Page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 7, lines 27-37 discloses the use of a cloned Q $\beta$  replicase binding site. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

137. A method of making a host cell resistant to a virus for the host, comprising:

Page 15, lines 34-35 discloses that the method of the invention is generally applicable to the protection of any host from a parasite of that host. "Host" is defined as any organism that can be infected by any parasitic organism. Page 15, lines 36-37. "Parasite" is defined as any organism that obtains substance or means for reproduction from an organism. Page 15, lines 37-40. "Resistance" is defined as any reduction in virulence of the parasitic infection or any reduction in the susceptibility of the host to the parasite. Page 4, lines 13-15.

Page 15, lines 54-57 discloses that plants (which are composed of cells and tissue) can be readily protected from viruses using the method of the invention. Page 15, lines 43-45 discloses that the preferable parasite is a DNA or RNA virus.

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isolating DNA coding for a gene, or fragment thereof, which encodes a protein or polypeptide of the virus other than a coat of protein or polypeptide;

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Page 16, lines 6-9 and lines 20-22 discusses how there are hundreds of significant plant RNA viruses, how essentially all crop species are affected by one or more such viruses, and how these are examples of host/parasite systems wherein resistance to the parasite can be given to the host. Page 16, lines 22-26 discloses that resistance to such viruses can be obtained by cloning fragments of the viruses into plant-transforming vectors and transforming the appropriate plants.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

"Gene" is defined to encompass both DNA sequences that code for peptide gene product and other DNA sequences that form a functional part of a chromosome or plasmid. Page 12, lines 23-26.

"Gene fragment" encompasses entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are incomplete parts of a single gene. Page 12, lines 19-23.

"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

Page 11, lines 63-66 states that, in general, genetic information (DNA or RNA) from any virus is isolated using standard procedures and cleaved into pieces of varying lengths.

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Page 12, lines 2-3 discloses that DNA fragments are typically obtained using restriction endonuclease enzymes.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection.

Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural, role. The example discusses expression of the coat protein under lac operator control. Page 18, lines 42-45. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); Page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 7, lines 27-37 discloses the use of a cloned Q $\beta$  replicase binding site. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

operably linking said DNA, or fragment thereof, within an expression vector in a sense direction; and

Page 12, lines 6-9 discloses that the vector can be a natural plasmid or transposon or any part thereof capable of replication in the host and, when desired, production of a gene product from the exogenous parasite gene fragment. Page 12, lines 11-13 discloses that the viral DNA is inserted into the vector using standard techniques in either a sense direction (when expression of a gene product is desired) or an antisense direction. Page 12, lines 14-17 discloses that proper tailoring of the gene fragment in the vector is readily achieved using standard techniques.

transforming said host cells with said expression vector.

Page 15, lines 8-10 discloses the transformation of plant cells.

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138. A method of making plant cells or plant tissue resistant to infection by one or more virus, comprising:

isolating DNA coding for a gene, or fragment thereof, which encodes a protein or polypeptide of the virus other than a coat protein or polypeptide;

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Page 15, lines 34-35 discloses that the method of the invention is generally applicable to the protection of any host from a parasite of that host. "Host" is defined as any organism that can be infected by any parasitic organism. Page 15, lines 36-37. "Parasite" is defined as any organism that obtains substance or means for reproduction from an organism. Page 15, lines 37-40. "Resistance" is defined as any reduction in virulence of the parasitic infection or any reduction in the susceptibility of the host to the parasite. Page 4, lines 13-15.

Page 15, lines 54-57 discloses that plants (which are composed of cells and tissue) can be readily protected from viruses using the method of the invention. Page 15, lines 43-45 discloses that the preferable parasite is a DNA or RNA virus.

Page 16, lines 6-9 and lines 20-22 discusses how there are hundreds of significant plant RNA viruses, how essentially all crop species are affected by one or more such viruses, and how these are examples of host/parasite systems wherein resistance to the parasite can be given to the host. Page 16, lines 22-26 discloses that resistance to such viruses can be obtained by cloning fragments of the viruses into plant-transforming vectors and transforming the appropriate plants.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

"Gene" is defined to encompass both DNA sequences that code for peptide gene product and other DNA sequences that form a functional part of a chromosome or plasmid. Page 12, lines 23-26.

"Gene fragment" encompasses entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are incomplete parts of a single gene. Page 12,



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"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

Page 11, lines 63-66 states that, in general, genetic information (DNA or RNA) from any virus is isolated using standard procedures and cleaved into pieces of varying lengths. Page 12, lines 2-3 discloses that DNA fragments are typically obtained using restriction endonuclease enzymes.

Page 7, lines 27-37 discloses the use of a cloned Q $\beta$  replicase binding site. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural, role. The example discusses expression of the coat protein under lac operator control. Page 18, lines 42-45. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); Page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely

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operably linking said DNA within an expression vector in a sense direction; and

transforming said plant cells or plant tissue with said expression vector.

139. A method of producing virus resistant plants comprising:

introducing into a plant cell a DNA coding for a gene, or fragment thereof, of the virus which when introduced into plant cells inhibits pathogenesis by the virus, wherein said DNA either (i) is in an anti-sense direction for expression of anti-sense RNA or (ii) is both in a sense direction and encodes a coat protein or polypeptide;

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analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 6-9 discloses that the vector can be a natural plasmid or transposon or any part thereof capable of replication in the host and, when desired, production of a gene product from the exogenous parasite gene fragment. Page 12, lines 11-13 discloses that the viral DNA is inserted into the vector using standard techniques in either a sense direction (when expression of a gene product is desired) or an antisense direction. Page 12, lines 14-17 discloses that proper tailoring of the gene fragment in the vector is readily achieved using standard techniques

Page 15, lines 8-10 discloses the transformation of plant cells.

Page 15, lines 54-57 discloses that plants can be readily protected from viruses using the method of the invention.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

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Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

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Page 5, line 66 to Page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural, role. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7. The example discusses expression of the coat protein under lac operator control. Page 18, lines 42-45. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

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recovering transformed plant cells; and

regenerating virus resistant plants from said transformed cells.

140. The method according to claim 139, wherein the DNA is in the sense direction and encodes a coat protein or polypeptide.

141. The method according to claim 139, wherein the DNA is in the anti-sense direction.

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Recovering transformed cells with increased resistance to Q $\beta$  infection is disclosed in the example discussed at Page 18, line 60 to page 19, line 39. See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 15, lines 11-12 indicates that whole transformed plants can be regenerated in numerous plant species.

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See also page 8, lines 12-19 (methods described for engineering resistance to Q $\beta$  would apply to essentially all viruses); page 16, lines 22-26 (resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria).

Page 12, lines 19-23 refers to "gene fragment" as encompassing entire genes, DNA segments that contain an entire gene or portion thereof, an segments of DNA that are incomplete parts of a single gene.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

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142. A recombinant DNA molecule comprising:

a promoter which is functional in plant cells; and

a DNA sequence, which encodes a protein or polypeptide native to a virus, operably linked to the promoter, wherein the DNA sequence either (i) is in an anti-sense direction for expression of anti-sense RNA or (ii) is both in a sense direction and encodes a coat protein or polypeptide, and wherein said recombinant DNA molecule, when introduced into the plant cells, will prevent the propagation of the virus.

143. The recombinant DNA molecule according to claim 142, wherein the DNA sequence is in the sense direction and encodes a coat protein or polypeptide.

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The example discloses a plasmid, which is a recombinant double-stranded DNA molecule. Page 18, lines 40-47.

Page 12, lines 14-17 refers to use of appropriate 5' sequences to ensure transcription (i.e., RNA production).

Page 12, lines 6-9 discloses that the vector can be a natural plasmid or transposon or any part thereof capable of replication in the host and, when desired, production of a gene product from the exogenous parasite gene fragment. Page 12, lines 11-13 discloses that the viral DNA is inserted into the vector using standard techniques in either a sense direction (when expression of a gene product is desired) or an antisense direction. Page 12, lines 14-17 discloses that proper tailoring of the gene fragment in the vector is readily achieved using standard techniques.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role. The example discusses expression of the coat protein under lac operator. Page 18, lines 42-45. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

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144. The recombinant DNA molecule according to claim 142, wherein the DNA sequence is in the anti-sense direction.

145. A virus resistant plant comprising:

a recombinant DNA molecule having a gene, or fragment thereof, isolated from a virus, wherein said gene, or fragment thereof, when introduced into plant cells either (i) is in an anti-sense direction for expression of anti-sense RNA or (ii) is both in a sense direction and encodes a coat protein or polypeptide of the virus, and wherein said gene, or fragment thereof, when introduced into plant cells inhibits pathogenesis by the virus.

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Page 7, lines 6-7.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

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endonuclease enzymes.

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Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

146. The virus resistant plant according to claim 145, wherein said gene or fragment thereof is in the sense direction and encodes a coat protein or polypeptide.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

147. The virus resistant plant according to claim 145, wherein said gene or fragment thereof is in the anti-sense direction.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

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148. A method of making a host cell resistant to a virus for the host, comprising:

isolating DNA coding for a gene, or fragment thereof, of said virus;

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Page 15, lines 34-35 discloses that the method of the invention is generally applicable to the protection of any host from a parasite of that host. "Host" is defined as any organism that can be infected by any parasitic organism. Page 15, lines 36-37. "Parasite" is defined as any organism that obtains substance or means for reproduction from an organism. Page 15, lines 37-40. "Resistance" is defined as any reduction in virulence of the parasitic infection or any reduction in the susceptibility of the host to the parasite. Page 4, lines 13-15.

Page 15, lines 54-57 discloses that plants (which are composed of cells and tissue) can be readily protected from viruses using the method of the invention. Page 15, lines 43-45 discloses that the preferable parasite is a DNA or RNA virus.

Page 16, lines 6-9 and lines 20-22 discusses how there are hundreds of significant plant RNA viruses, how essentially all crop species are affected by one or more such viruses, and how these are examples of host/parasite systems wherein resistance to the parasite can be given to the host. Page 16, lines 22-26 discloses that resistance to such viruses can be obtained by cloning fragments of the viruses into plant-transforming vectors and transforming the appropriate plants.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

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"Gene fragment" encompasses entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are



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operably linking said DNA, or fragment thereof, within an expression vector, wherein said DNA either (i) is in an anti-sense direction or (ii) is both in a sense direction and encodes a coat protein or polypeptide of said virus; and

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incomplete parts of a single gene. Page 12, lines 19-23.

"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

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transforming said host cells with said expression vector.

149. The method according to claim 148, wherein said DNA or fragment thereof is in the sense direction and encodes a coat protein or polypeptide.

150. The method according to claim 148, wherein said DNA or fragment thereof is in the anti-sense direction.

151. A method of making plant cells or plant tissue resistant to infection by one or more virus, comprising:

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will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

Page 15, lines 8-10 discloses the transformation of plant cells.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

Page 15, lines 34-35 discloses that the method of the invention is generally applicable to the protection of any host from a parasite of that host. "Host" is defined as any organism that can be infected by any parasitic organism. Page 15, lines 36-37. "Parasite" is defined as any organism that obtains substance or means for reproduction from an organism. Page 15, lines 37-40. "Resistance" is defined as any reduction in virulence of the parasitic infection or any reduction in the susceptibility of the host to the parasite. Page 4, lines 13-15.

Page 15, lines 54-57 discloses that plants (which are composed of cells and tissue) can be readily protected from viruses using the method of the invention. Page 15, lines 43-45 discloses that the preferable parasite is a DNA or RNA virus.

Page 16, lines 6-9 and lines 20-22 discusses how there are hundreds of significant plant

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isolating DNA coding for a gene, or fragment thereof, of said virus;

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RNA viruses, how essentially all crop species are affected by one or more such viruses, and how these are examples of host/parasite systems wherein resistance to the parasite can be given to the host. Page 16, lines 22-26 discloses that resistance to such viruses can be obtained by cloning fragments of the viruses into plant-transforming vectors and transforming the appropriate plants.

Page 15, lines 54-57 discloses that host resistance to a particular parasite can effectively be engineered by introducing a gene, gene fragment, or modified gene or gene fragment of the pathogen into the host.

"Gene" is defined to encompass both DNA sequences that code for peptide gene product and other DNA sequences that form a functional part of a chromosome or plasmid. Page 12, lines 23-26.

"Gene fragment" encompasses both entire genes, DNA segments that contain an entire gene or a portion thereof, and segments of DNA that are incomplete parts of a single gene. Page 13, lines 19-23.

"Isolated" is used to indicate that a gene has been obtained in a useful form by a deliberate process. Page 13, lines 14-16. "Isolating a gene fragment" is defined as referring to the process of obtaining a gene fragment to be used in the production of resistance in a useful form. Page 13, lines 9-12.

Page 12, lines 36-38 discloses that use of cDNA prepared from RNA is a preferred embodiment of the invention when producing resistance to an RNA virus.

Page 11, lines 63-66 states that, in general, genetic information (DNA or RNA) from any virus is isolated using standard procedures and cleaved into pieces of varying lengths. Page 12, lines 2-3 discloses that DNA fragments are typically obtained using restriction

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operably linking said DNA, or fragment thereof, within an expression vector, wherein said DNA either (i) is in an anti-sense direction or (ii) is both in a sense direction and encodes a coat protein or polypeptide of said virus; and

transforming said plant cells or plant tissue with said expression vector.

152. The method according to claim 151, wherein said DNA or fragment thereof is in the sense direction and encodes a coat protein or polypeptide.

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endonuclease enzymes.

Page 12, lines 6-9 discloses that the vector can be a natural plasmid or transposon or any part thereof capable of replication in the host and, when desired, production of a gene product from the exogenous parasite gene fragment. Page 12, lines 11-13 discloses that the viral DNA is inserted into the vector using standard techniques in either a sense direction (when expression of a gene product is desired) or an antisense direction. Page 12, lines 14-17 discloses that proper tailoring of the gene fragment in the vector is readily achieved using standard techniques.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

Page 15, lines 8-10 discloses the transformation of plant cells.

Page 5, line 66 to page 6, line 2 discusses how the genes of the bacteriophage Q $\beta$  can be used to make E. coli resistant to Q $\beta$  infection. Page 6, lines 8-11 discloses that the Q $\beta$  genome has three major cistrons; these code for a maturation protein, a coat protein, and a subunit of the replicase enzyme. Page 6, lines 67-68 discloses that the coat protein is known to have a regulatory, as well as a structural role. Expression of coat protein in the host will repress any replication of an infecting Q $\beta$ . Page 7, lines 6-7.

Page 12, lines 11-13 discloses where the viral DNA is inserted in the sense direction.

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153. The method according to claim 151, wherein said DNA or fragment thereof is in the anti-sense direction.

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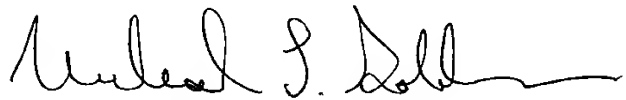
Page 12, lines 11-13 discloses where the viral DNA is inserted in the anti-sense direction.

The only amendment to reissue claims 31, 61-64, 66, 69, 70, 72, 77, 78, 80, 82, 105-112, 117, 118, 120, 121, 125, 126, 131, and 132 was in their claim dependency. With respect to claim 114, the claim dependency was amended and the language "a product" (line 4) was replaced by "said protein or polypeptide" to correct for antecedent basis resulting from the changed claim dependency.

Claim 29 was amended by introducing "virus-resistant" after "transformed" (line 1). Descriptive support for this amendment is provided at page 15, lines 54-57, which indicates that plants can readily be protected from viruses using the method of the present invention.

Claim 37 was amended by introducing "wherein the recombinant double-stranded DNA molecule, when introduced into a plant cell, inhibits pathogenic activity of said plant virus" after "sequence" (line 8). Descriptive support for this amendment is provided at page 18, lines 41-45, which discloses expression of Q $\beta$  coat protein in *E. coli*; page 8, lines 12-19, which recites that the methods described for engineering resistance to Q $\beta$  would apply essentially to all viruses; and page 16, lines 22-26, which recites that resistance to RNA plant viruses can be obtained in a manner closely analogous to Q $\beta$  resistance in bacteria.

Respectfully submitted,



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Date: July 2, 1999

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